08/466,921

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DATE MAILED: 11/28/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 06/06/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-22 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 3, 4, 8, 13, 14, and 18-22 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1, 2, 5-7, 9-12, and 15-17 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☒ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Detailed Office Action

15. Acknowledgement is hereby made of Paper No. 2 containing the preliminary amendment. In the instant application claims 3-4, 8, 13, 14, and 18-22 have been canceled without prejudice or disclaimer while claims 1, 2, 5-7, 9-12, and 15-17 are currently pending.

16. Acknowledgement is hereby made of applicants' claim for domestic priority under 35 U.S.C. § 120 based upon a series of applications dating to Serial No. 06/558,109, filed December 05, 1983. Perusal of these applications demonstrated that the nucleic acids recited in claims 1, 2, 5-7, and 9-12 receive support in application Serial No. 06/771,230, filed August 30, 1985. Accordingly, the claimed material will receive the corresponding priority date. Claims 15-17, directed towards nucleic acids encoding for the core proteins, reverse transcriptase (RT), and envelope proteins, do not receive support in the earlier filed applications. Accordingly, these claims will receive the priority date of the instant application. Applicants have also requested foreign priority under 35 U.S.C. § 119 corresponding to a United Kingdom application, Serial No. 84 23659, filed September 19, 1994. A certified copy of the foreign priority document was presumably placed in a prior related application. However, at the time of this office action this foreign priority document was not available for review. Submission of this document would facilitate the evaluation of the applicants' claim to foreign priority.

17. The drawings filed in this application are objected to by the Draftsperson under 37 C.F.R. 1.84 or 1.152 as indicated. These informal drawings are acceptable for examination purposes only. Formal drawings with the appropriate corrections will be required when the application is allowed.

18. The applicants are reminded of the proper language and format of an Abstract of the Disclosure as follows:

> The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said", should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title.

The claimed invention is directed towards novel nucleic acids useful for the detection of human immunodeficiency viruses (HIV). A series of recombinant cDNA clones were generated from purified LAV obtained from a LAV-infected cell line. LAV-containing lambda phage clones were also obtained from the genomic DNA of a LAV-infected patient. The aforementioned clones were subjected to restiction analyses and their relationship to human T-cell leukemia viruses 1 and 2 determined. A more comprehensive abstract that accurately portrays the specified embodiment of the invention is required.

19. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. The specification is objected to under 35 U.S.C. § 112, first paragraph, as the disclosure is not commensurate with the scope of the claims. Claims 1, 2, 5-7, 9-12, and 15-17, are directed towards cloned DNAs capable of hybridizing with the genomic RNA of LAV. The broadly recited claim language encompasses DNA fragments, of either viral or cellular origin, displaying disparate lengths that are derived from a multitude of sources (i.e. general cloning vector, lambda phage vector, transcription vector, sequencing vector, etc.). However, the specification only teaches the isolation of the cloned LAV DNAs consisting of pLAV75, pLAV82, pLAV13, λJ19 and λJ81. Applicants should amend the claim language to identify those fragments supported by the specification.

Claims 15-17 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

21. The specification is further objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention. Claims 15-17 are directed towards DNA fragments capable of encoding for the LAV envelope proteins, reverse transcriptase, and core proteins. The specification discloses the preliminary restriction analysis of lambda phage clones (e.g. λJ19 and λJ81) and cDNA clones (e.g. pLAV75, pLAV82, and pLAV13). The

specification is silent pertaining to the disclosure of those regions of the viral genome capable of encoding for the indicated viral proteins. The applicants merely surmise as to which restriction fragments contain viral coding regions. The demonstration of a bona fide viral open reading frame requires the generation of specific immunological reagents (i.e. monoclonal or polyclonal antibodies) towards the protein of interest and identification of the protein, either in cellular or viral preparations.

Claims 15-17 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

22. Claims 1, 2, 5-7, 9-12, and 15-17 are rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is directed towards a "cloned DNA" containing DNA hybridizable to the RNA genome of LAV. This phrase is confusing since it is not readily manifest what type of cloned DNA is encompassed by the claim language (i.e. a cloning vector, sequencing vector, transcription vector, expression vector, reporter vector, lambda phage vector, specialized vector, etc.). Claims 5 and 6 recite restriction sites and contain the additional parenthetical designations (LAV 82) and (LAV 13), respectively. This recitation is confusing and should be amended accordingly. The recitation of "a size about", "from about", and "approximately" in claims 7, 9, 11, and 12 does not adequately disclose the metes and bounds of the claimed invention. Applicants should clarify the claim language by including a description of the vector (i.e. pBR322), the precise viral fragment

or insert (cloning sites and nucleotide sequence) contained therein (i.e. the DNA consisting of pLAV75, which contains a 600bp *Pst*I-*Pst*I fragment in pBR322), and the correct orientation of the restriction sites (i.e. "The DNA containing the restriction sites *Hind*III, *Sac*I, and *Bgl*II, reading 5' to 3' on the coding strand").

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent; and
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

25. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

26. Claims 1, 2, 5-7, and 9-12, directed towards cloned DNAs capable of hybridizing with the genomic RNA of the LAV viruses, are rejected under 35 U.S.C. § 102(a) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as being unpatentable over Arya et al. (1984, Science 225:927-930).

Arya et al. (1984) teach the generation of cloned DNAs (cDNAs) obtained from human T-cell leukemia virus type III (HTLV-III) isolated from AIDS patients. The HTLV-III virus displays cytopathicity towards T-lymphocytes, reverse transcriptase activity, and a p24 core antigen. The authors also reported that "Using the infected cells as well as purified virus particles in immunological assays, we found that the serum of 80 to 100 percent of AIDS patients and 70 to 80 percent of patients with lymphadenopathy syndrome reacted positively" (refer to paragraph 2 on page 927).

Arya et al. (1984) further teach the generation of cDNA probes

useful for hybridization purposes. The authors reported the following (refer to page 928 and Figures 1 and 2):

> Virus particles were also purified from normal peripheral blood lymphocytes newly infected by virus of a primary leukocyte culture of another AIDS patient ($HTLV\text{-}III_Z$) (11). The particles were lysed with sodium dodecyl sulfate (SDS), digested with proteinase K, and directly chromatographed on an oligo(dT) cellulose column. The resulting polyadenylate [poly(a)-containing RNA was used as template to synthesize ^{32}P-labeled complementary DNA (cDNA) in the presence of oligo(dT) primers. The size of the resultant cDNA ranged from 0.1 to 10 kb (not shown). When these labeled cDNA's were hybridized to poly(A)-containing RNA purified from infected and uninfected H9 cells as well as other uninfected human cell lines, on ly the infected H9 cells contained homologous RNA sequences as evidenced by discrete RNA bands after Northern hybridization. Figure 1 shows that cDNA preparations from $HTLV\text{-}III_B$ and $HTLV\text{-}III_Z$ gave identical patterns, detecting RNA species of about 9.0, 4.2, and 2.0 kb. These bands are similar in size to those corresponding to genomic size messenger RNA (mRNA) and spliced mRNAs of *env* ...

Finally, the authors also indicated that a family of related AIDS viruses may exist. Specifically, Arya et al. (1984) reported (column 1, page 929) that "Retroviruses called LAV (or sometimes $IDAV_1$ or $IDAV_2$) have been isolated from patients with lymphadenopathy syndrome and AIDS (17). Although LAV has been reported to lack relatedness to HTLV-I and -II (17), further characterization of its proteins and nucleic acids may reveal that LAV is related to these viruses and is identical to or related to HTLV-III."

Although Arya et al. (1984) do not recite the specific restriction sites of the instant invention, one skilled in the art would anticipate, *a priori*, that a closely related family of viruses would inherently contain the same restriction map. Since the Patent Office does not have the facilities for examining and comparing applicants' DNA with the cDNA constructs of the prior art reference, the burden is

upon applicants to show an unobvious distinction between the material, structural, biochemical, and functional characteristics of the claimed DNAs and the cDNA of the prior art (refer to In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 1977)). Manifestly, the disclosure by Arya et al. (1984) satisfies the limitations of the claimed invention.

27. Claims 1, 2, 5-7, and 9-12, directed towards cloned DNAs capable of hybridizing with the genomic RNA of the LAV viruses, are rejected under 35 U.S.C. § 102(e) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as being unpatentable over Levy (1987, US PAT No. 4,716,102).

Levy (1987) discloses the identification of a novel family of human retroviruses associated with AIDS, designated AIDS-associated viruses (ARV). Said viruses were isolated from AIDS patients and displayed Mg^{2+}-dependent RT activity and a T-lymphocyte tropism. The '102 patent also suggests that HTLV-III, LAV, and ARV are all members of a family of retroviruses implicated in AIDS or lymphadenopathy syndrome (LAS). Levy (1987) teaches the propagation, isolation, and purification of ARV. The utilization of cDNA fragments as hybridization probes is also clearly taught. It was reported that (columns 4 and 5):

> ARV-derived polynucleic acid for use in making probes may be obtained from ARV particles or chronically infected HUT-78 cells. Nucleic acids are liberated from the particles or cells, isolated, and digested with one or more restriction enzymes to produce nucleic acid fragments of appropriate size. Particular fragments may be isolated from the digest by gel electrophoresis, if desired. The desired fragments may be replicated by cloning them into a suitable vector (prokaryotic or eukaryotic) to form a replicon. ... The fragments may be recovered from the host by extracting nucleic acids with the same endonuclease(s) used previously and resolving the digest, such as be electrophoresis, to isolate the desired fragment(s).

> The fragments may be labeled by conventional techniques. ... ^{32}P is a preferred label. The fragments may be labeled with ^{32}P by nick translation with a α-^{32}P-dNTP or other ^{32}P labeling procedure.

The aforementioned virus appears to have the same biochemical, immunological, and virological properties as the applicants disclosed virus. One would anticipate, *a priori*, that the virus disclosed by this teaching would contain all the inherent characteristics of the applicants' instantly claimed invention, including the recited restriction sites. Since the Patent Office does not have the facilities for examining and comparing applicants' DNA with the cDNA constructs of the prior art reference, the burden is upon applicants to show an unobvious distinction between the material, structural, biochemical, and functional characteristics of the claimed DNAs and the cDNA of the prior art (refer to In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 1977)). Accordingly, the disclosure by Levy (1987) satisfies the limitations of the claimed invention.

28. Claims 15-17, directed towards cloned LAV DNAs capable of encoding for the envelope, polymerase, and core proteins, are rejected under 35 U.S.C. § 102(b) as being anticipated by Wain-Hobson et al. (1985, Cell 40:9-17).

Wain-Hobson et al. (1985) disclose the complete 9193-nucleotide sequence of the lymphadenopathy associated virus (LAV). Proviral genomic clones (e.g. λJ19 and λJ81) and cDNA clones (e.g. pLAV75) were subjected to nucleotide sequence analysis. These are the same clones recited in the instant application (refer to Figures 1 and 2). This teaching specifically identifies the corresponding genomic regions encoding for the *gag*, *pol*, and *env* proteins. It was further emphasized

that the identification of a full-length proviral clone of LAV would be of "obvious diagnostic and therapeutic potential".

29. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Group 1813 is **(703) 305-7939.**

30. Any inquiry concerning this communication should be directed to **Jeffrey S. Parkin, Ph.D.** whose telephone number is **(703) 308-2227.** The examiner can normally be reached Monday through Friday from 8:30 AM to 5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, **Ms. Christine Nucker** can be reached at **(703) 308-4028.** Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Group Art Unit 1813

November 16, 1995

ROBERT D. BUDENS
PRIMARY EXAMINER
GROUP 1800